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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/628,126 | 07/28/2000 | Raymond G. Goodwin | 2804-1 | 3935 |

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| ART UNIT | PAPER NUMBER |
|---|---|
| 1642 | |

DATE MAILED: 01/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/628,126 | GOODWIN ET AL. | |
| | Examiner | Art Unit | |
| | Sheela J Huff | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 October 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *27-30,32,33,38-40,42,43,50-66 and 68-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-30,32,33,38-40,42,43,50-66 and 68-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

The amendment filed on 10/23/02 has been considered. Applicant's arguments are deemed to be persuasive-in-part.

Claims 27-30, 32-33, 38-40, 42-43, 45, 50-66 and 68-70 are pending.

All of the rejections, except for the last 103 rejection, have been withdrawn in view of applicant's amendment. The last 103 rejection is withdrawn in favor of a new one.

***Information Disclosure Statement***

The Dallenbach et al reference and the Stein reference has been considered. A copy of the initialed PTO-1449 is enclosed.

***New Grounds of Rejection***

***Claim Rejections - 35 USC § 112***

Claims 27-30, 32-33, 38-40, 42-43, 45, 50-66 and 68-70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 42 and 45 depend on cancelled claim 36. No art has been applied to these claims because the Examiner could not determine the independent claim.

b. Claims 27 and 28 refer to amino acids 19-390 of SEQ ID NO. 1. However, SEQ ID No. 1 is a nucleic acid sequence not an amino acid sequence. It is assumed that applicant meant SEQ ID No. 2 and such a correction is requested. The following rejections are based on this assumption.

Claims 27, 32, 33, 38, 40, 50-66 and 68-70 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polypeptides having at least 90% identity with aa 49-220 of SEQ ID no. 19 or aa 47-215 of 23. While the amino acid sequences of aa 49-220 of SEQ ID no. 19 or aa 47-215 of 23 are adequately described in the specification as-filed, thereby providing an adequate basis for the polypeptide; there is insufficient written description as to the identity of a polypeptide having at least 90% identity with aa 49-220 of SEQ ID no. 19 or aa 47-215 of 23 that would still maintain the function of the polypeptide. Consequently, the specification does not provide an adequate written description of a polypeptide having at least 90% identity with aa 49-220 of SEQ ID no. 19 or aa 47-215 of 23.

The specification as filed does not provide adequate written description support for an antibody to a polypeptide having at least 90% identity with aa 49-220 of SEQ ID no. 19 or aa 47-215 of 23. Polypeptides having diverse functions are encompassed by the phrase. Thus a broad genus having potentially highly diverse functions is encompassed by the phrase at least 90% identity with aa 49-220 of SEQ ID no. 19 or aa 47-215 of 23 and conception cannot be achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. For example,

Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Adequate written description requires more than a mere statement that it is part of the invention. The sequence itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

Therefore, only aa 49-220 of SEQ ID no. 19 or aa 47-215 of 23 meet the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 27-30, 32-33, 38-40, 42-43, 45, 50-66 and 68-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thorpe US 5165923 in view of Verheul WO 92/00762, Smith et al Cell 73:1349 (7/2/93), Goodwin et al WO 93/24135, applicant admission on page 15 of the specification and Stein et al DE 4200043 (5/13/93) (US 5866372 is the English equivalent of the DE document).

Thorpe et al teach a method of delivering a therapeutic agent to CD30+ cells comprising contacting said cells with a conjugate comprising toxins (reads on therapeutic agents) such as ricin, diptheria, abrin, P. exotoxin A and ribosomal inactivating proteins, such as saponin, attached to an anti-CD30 ab for the treatment of Hodkin's disease and lymphomas associated with CD30+ lymphocytes (see abstract, col. 1 para. 4, col. 2 para. 1-2, col. 7 para. 2-3 and 5, col. 8 para. 2 and claims 1, 11-13 17-19 and 23-24). This patent also stresses that their invention is not limited to the use ab, but also prepare other binding ligands that have a suitable degree of binding affinity (col. 4, lines 50+).

The only differences between the instant application and the reference is the use of soluble CD30L ( SEQ ID No. 19, 22 or 23), the CD30 being aa 19-390 of SEQ ID NO. 1 (2?), the specific oligomers of claims 32-33 and 69 and the therapeutic agents of claims 50-66 and 70.

Verheul et al discloses the use of targeting toxins to receptors using antibodies fragments thereof or using natural ligand receptor for the receptor or fragment thereof to the toxin for the treatment of tumor cells (p. 2, para 4-5, page 1, para. 2-3).

Smith et al and Goodwin et al both disclose the nucleic and amino acid sequence of CD30L membrane-bound and soluble CD30L polypeptide having the Seq ID 19, 22 or 23 see claims 15-16, 18, 19-20 and figures 3a, 5a, 6a and 7a) (see attached sequence alignment for SEQ ID No. 22 comparison). Goodwin et al goes on to disclose that the CD30L polypeptide binds to CD30, which is found on Hodgkin's disease tumor cells and lymphomas (abstract and page 1, para 1). The CD30L has a therapeutic potential (page 3, lines 29-30) and the CD30L includes full length and truncated proteins which retain binding activity (page 4, lines 11-14 and page 7) and CD30L can be modified to form covalent aggregates with other moieties and can exist as oligomers (page 9 and 13). The oligomers of CD30L can be expressed as fusion proteins linked to an IgG Fc region (page 13).

Stein et al disclose that CD30, which reads on aa 19-390 of Seq ID No. 2, is known in the art and is a lymphoid antigen occurring in Hodgkin's disease (abstract and Seq ID No. 2 of reference (see attached sequence alignment for SEQ ID No. comparision).

On page 15 of the specification, applicant admits that the therapeutic agents of claims 50-66 and 70 are known in the art.

Thus, in view of Verheul, which states that either ab or natural ligand can be linked to toxin, it would have been obvious to one of ordinary skill in the art at the time of

applicant's invention to use the ligand for CD30 in place of the ab in the primary reference. The newly formed conjugate would be effective in the treatment of Hodgkin's disease. Goodwin et al and Smith et al both show that the ligand for CD30, which is CD30L, is known in the art. Since Stein et al shows that an antigen on the surface of lymphoid cells has the sequence of SEQ ID No. 2, it would be obvious that the newly formed conjugate CD30L-toxin would bind to SEQ Id no. 2. The use of any of the therapeutic agents of claims 50-66 and 70 is within the purview of one skilled in the art since the use of any of these is well known in the art.

Response to applicant's arguments to the extent that they apply to the above rejection

Applicant argues that WO 93/24135 is not valid prior art. Applicant states that all of the inventors on the WO are on the instant application. It is noted that there is one more inventor on the instant application (ie Gruss) and thus since the inventive entities are different the reference is valid prior art.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J Huff whose telephone number is 703-305-7866. The examiner can normally be reached on T,Th 6am-12pm and alternate Mondays 6am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Sheela J Huff
Primary Examiner
Art Unit 1642

sjh
December 31, 2002